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October 15, 2002

p#6

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October 15, 2002	<i>Michael R. Krawzsenek</i>
Date	Michael R. Krawzsenek

Commissioner for Patents
Washington, DC 20231

Re: *U.S. Patent Application No. 10/039,171 entitled "COMPOSITIONS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF ORGANOPHOSPHATE TOXICITY" by Robert Haley et al.*
Our Reference: UTSD:749US
Client Reference: UTSMD/DAL:0749

Sir:

Enclosed for filing in the above-referenced patent application is an Information Disclosure Statement, Form PTO-1449, and references (C1-C62).

No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to the enclosed materials, the Commissioner is hereby authorized to deduct said fees from Fulbright & Jaworski Deposit Account No.: 50-1212/UTSD:749US.

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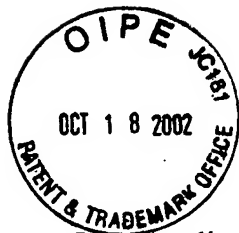
Respectfully submitted,

Michael R. Krawzsenek

Michael R. Krawzsenek
Reg. No. 51,898

MRK/cmb
Encl.: as noted

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of:
Robert Haley *et al.*

Serial No.: 10/039,171

Filed: January 3, 2002

For: COMPOSITIONS AND METHODS FOR
THE DIAGNOSIS AND TREATMENT OF
ORGANOPHOSPHATE TOXICITY

Group Art Unit: 1645

Examiner: Unknown

Atty. Dkt. No.: UTSD:749US

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Michael R. Krawczsenek
Michael R. Krawczsenek

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

In compliance with the duty of disclosure under 37 C.F.R. § 1.56, it is respectfully requested that this Information Disclosure Statement be entered and the documents listed on attached Form PTO-1449 be considered by the Examiner and made of record. Copies of the listed documents required by 37 C.F.R. § 1.98(a)(2) are enclosed for the convenience of the Examiner.

In accordance with 37 C.F.R §§ 1.97(g), (h), this Information Disclosure Statement is not to be construed as a representation that a search has been made, and is not to be construed to be an admission that the information cited is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

The present Information Disclosure Statement is being filed prior to the receipt of a first Official Action reflecting an examination on the merits, and hence is believed to be timely filed in accordance with 37 C.F.R § 1.97(b). No fees are believed to be due in connection with the filing of this Information Disclosure Statement, however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be deemed necessary for any reason relating to these materials, the Commissioner is hereby authorized to deduct said fees from Fulbright & Jaworski Deposit Account No.: 50-1212/UTSD:749US.

Applicants respectfully request that the listed documents be made of record in the present case.

Respectfully submitted,



Michael R. Krawwsenek
Reg. No. 51,898
Attorney for Applicants

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Date: October 15, 2002

Form PTO-1449 (modified)

Atty. Docket No.

Serial No.

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U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.

Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No

Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Abou-Donia <i>et al.</i> , "Increased neurotoxicity following concurrent exposure to pyridostigmine bromide, DEET, and chlorpyrifos," <i>Fund. Appl. Toxicol.</i> 34:201-222, 1996.
	C2	Adkins <i>et al.</i> , "Molecular basis for the polymorphic forms of human serum paraoxonase/arylesterase: glutamine or arginine at position 191, for the respective A or B allozymes," <i>Am. J. Hum. Genet.</i> , 52:598-608, 1993.
	C3	Aldridge "An enzyme hydrolyzing diethyl p-nitrophenol phosphate (E600) and its identity with the A-esterase of mammalian sera," <i>Biochem. J.</i> , 53:117-124, 1953.
	C4	Betarbet <i>et al.</i> , "Chronic systemic pesticide exposure reproduces features of Parkinson's disease," <i>Nature Neuroscience</i> , 3:1301-1306, 2000.
	C5	Bharucha <i>et al.</i> , "Geographic distribution of motor neuron disease and correlation with possible etiologic factors," <i>Neurology</i> , 33:911-915, 1983.
	C6	Broomfield <i>et al.</i> , "Protection by butyrylcholinesterase against organophosphorus poisoning in nonhuman primates," <i>J. Pharm. Exper. Ther.</i> , 259:633-638, 1991.
	C7	Cao <i>et al.</i> , "Paraoxonase protection of LDL against peroxidation is independent of its esterase activity towards paraoxon and is unaffected by the Q-->R genetic polymorphism," <i>J. Lipid Res.</i> , 40:133-139, 1999.
	C8	Caroscio <i>et al.</i> , "Amyotrophic lateral sclerosis: its natural history," <i>Neurol. Clin.</i> , 5:1-8, 1987.

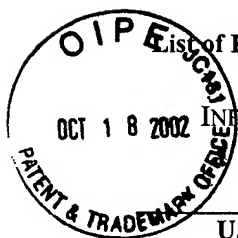
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Applicant
Robert Haley, *et al.*Filing Date:
January 3, 2002Group:
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Exam. Init.	Ref. Des.	Citation
	C9	Checkoway <i>et al.</i> , "Genetic polymorphisms in Parkinson's disease," <i>Neurotoxicology</i> , 19:635-643, 1998.
	C10	Clendenning <i>et al.</i> , "Structural organization of the human <i>PON1</i> gene," <i>Genomics</i> , 35:586-589, 1996.
	C11	Costa and Manzo, "Biochemical markers of neurotoxicity: research strategies and epidemiological applications," <i>Toxicology Letters</i> , 77:137-144, 1995.
	C12	Costa <i>et al.</i> , "Serum paraoxonase and its influence on paraoxon and chlorpyrifos-oxon toxicity in rats," <i>Toxicol. Appl. Pharmacol.</i> , 103:66-76, 1990.
	C13	Costa <i>et al.</i> , "The role of paraoxonase (PON1) in the detoxication of organophosphates and its human polymorphism," <i>Chem. Biol. Interact.</i> , 119-120:429-438, 1999.
	C14	Davies <i>et al.</i> , "The effect of the human serum paraoxonase polymorphism is reversed with diazoxon, soman and sarin," <i>Nat. Genet.</i> , 14:334-336, 1996.
	C15	Doctor <i>et al.</i> , "Cholinesterases as scavengers for organophosphorus compounds: protection of primate performance against soman toxicity," <i>Chem. Biol. Interact.</i> , 87:285-293, 1993.
	C16	Doctor <i>et al.</i> , "Enzymes as pretreatment drugs for organophosphate toxicity," <i>Neuroscience and Biobehavioral Reviews</i> , 15:123-128, 1991.
	C17	Dunn and Sidell, "Progress in medical defense against nerve agents," <i>JAMA</i> , 262:649-652, 1989.
	C18	Eckerson <i>et al.</i> , "The human serum paraoxonase polymorphism: identification of phenotypes by their response to salts," <i>Am. J. Hum. Genet.</i> , 35:214-227, 1983.
	C19	Eckerson <i>et al.</i> , "The human serum paraoxonase/arylesterase polymorphism," <i>Am. J. Hum. Genet.</i> , 35:1126-1138, 1983.
	C20	Feingold <i>et al.</i> , "Paraoxonase activity in the serum and hepatic mRNA levels decrease during the acute phase response," <i>Atherosclerosis</i> , 139:307-315, 1998.
	C21	Gan <i>et al.</i> , "Purification of human serum paraoxonase/arylesterase," <i>Drug Metab. Dispos.</i> , 19:100-106, 1991.
	C22	Gray, "Design and structure-activity relationships of antidotes to organophosphorous anticholinesterase agents," <i>Drug Metabolism Reviews</i> , 15:557-589, 1984.

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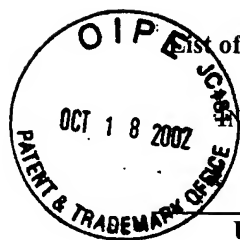
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/	C23	Haley and Kurt, "Self-reported exposure to neurotoxic chemical combinations in the Gulf War: a cross-sectional epidemiologic study," <i>JAMA</i> , 277:231-237, 1997.
/	C24	Haley <i>et al.</i> , "Association of low PON1 type Q (type A) arylesterase activity with neurologic symptom complexes in Gulf War veterans," <i>Toxicol. Appl. Pharm.</i> , 157:227-233, 1999.
/	C25	Hassett <i>et al.</i> , "Characterization of cDNA clones encoding rabbit and human serum paraoxonase: the mature protein retains its signal sequence," <i>Biochemistry</i> , 30:10141-10149, 1991.
/	C26	Humbert <i>et al.</i> , "The molecular basis of the human serum paraoxonase activity polymorphism," <i>Nature Genet.</i> , 3:73-76, 1993.
/	C27	Husain <i>et al.</i> , "A comparative study of delayed neurotoxicity in hens following repeated administration of organophosphorus compounds," <i>Indian J. Physiol. Pharmacol.</i> , 39:47-50, 1995.
/	C28	Husain <i>et al.</i> , "Delayed neurotoxic effect of sarin in mice after repeated inhalation exposure," <i>J. Appl. Toxicol.</i> , 13:143-145, 1993.
/	C29	Ikeda <i>et al.</i> , "Serum paraoxonase activity and its relationship to diabetic complications in patients with non-insulin-dependent diabetes mellitus," <i>Metabolism</i> , 47:598-602, 1998.
/	C30	Kao <i>et al.</i> , "A variant of paraoxonase (PON1) gene is associated with diabetic retinopathy in IDDM," <i>J. Clin. Endocrinol. Metab.</i> , 83:2589-2592, 1998.
/	C31	Keeler <i>et al.</i> , "Pyridostigmine used as a nerve agent pretreatment under wartime conditions," <i>JAMA</i> , 266:693-695, 1991.
/	C32	Konda and Yamamoto, "Genetic polymorphism of paraoxonase 1 (PON1) and susceptibility to Parkinson's disease," <i>Brain Research</i> , 806:271-273, 1998.
/	C33	La Du <i>et al.</i> , "Serum paraoxonase (PON1) isozymes: the quantitative analysis of isozymes affecting individual sensitivity to environmental chemicals," <i>Drug Metab. Dispos.</i> , 29(4, Part 2): 566-569, 2001.
/	C34	La Du, "Human serum paraoxonase/arylesterase," In: Kalow W, editor. <i>Pharmacogenetics of Drug Metabolism</i> . New York: Pergamon Press, Inc.; p. 51-91, 1992.
/	C35	Langston, "Epidemiology versus genetics in Parkinson's disease: progress in resolving an age-old debate," <i>Ann. Neurol.</i> , 44 (Suppl 1):S45-S52, 1998.

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	C36	Le Couteur <i>et al.</i> , "Pesticides and Parkinson's disease," <i>Biomed. Pharmacother.</i> , 53:122-130, 1999.
	C37	Li <i>et al.</i> , "Serum paraoxonase status: a major factor in determining resistance to organophosphates," <i>J. Toxicol. Environ. Health</i> , 40:337-346, 1993.
	C38	Li <i>et al.</i> , "Muscarinic receptor-mediated pyridostigmine-induced neuronal apoptosis," <i>Neurotoxicology</i> , 21:541-552, 2000.
	C39	Li <i>et al.</i> , "Paraoxonase protects against chlorpyrifos toxicity in mice," <i>Toxicology Letters</i> , 76:219-226, 1995.
	C40	Loewenstein-Lichtenstein <i>et al.</i> , "Genetic predisposition to adverse consequences of anti-cholinesterases in 'atypical' BChE carriers," <i>Nature Med.</i> , 1:1082-1085, 1995.
	C41	Lorentz <i>et al.</i> , "Arylesterase in serum: elaboration and clinical application of a fixed-incubation method," <i>Clin. Chem.</i> , 25/10:1714-1720, 1979.
	C42	Mackness <i>et al.</i> , "Effect of the molecular polymorphisms of human paraoxonase (PON1) on the rate of hydrolysis of paraoxon," <i>Br. J. Pharmacol.</i> , 122:265-268, 1997.
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	C44	Mackness <i>et al.</i> , "Serum paraoxonase (PON1) 55 and 192 polymorphism and paraoxonase activity and concentration in non-insulin dependent diabetes mellitus," <i>Atherosclerosis</i> , 139:341-349, 1998.
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	C46	McGuire <i>et al.</i> , "Occupational exposures and amyotrophic lateral sclerosis: a population-based case-control study," <i>Am. J. Epidemiol.</i> , 145:1076-1088, 1997.
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	C48	Odawara <i>et al.</i> , "Paraoxonase polymorphism (Gln192-Arg) is associated with coronary heart disease in Japanese noninsulin-dependent diabetes mellitus," <i>J. Clin. Endocrinol. Metab.</i> , 82:2257-2260, 1997.
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/	C50	Pfohl <i>et al.</i> , "Paraoxonase 192 Gln/Arg gene polymorphism, coronary artery disease, and myocardial infarction in type 2 diabetes," <i>Diabetes</i> , 48:623-627, 1999.
/	C51	Playfer <i>et al.</i> , "Genetic polymorphism and interethnic variability of plasma paraoxonase activity," <i>J. Med. Genet.</i> , 13:337-342, 1976.
/	C52	Poirier <i>et al.</i> , "Environment, genetics and idiopathic Parkinson's disease," <i>Can. J. Neurol. Sci.</i> , 18:70-76, 1991.
/	C53	Primo-Parmo <i>et al.</i> , "The human serum paraoxonase/arylesterase gene (PON1) is one member of a multigene family," <i>Genomics</i> , 33:498-507, 1996.
/	C54	Sakai <i>et al.</i> , "Serum paraoxonase activity and genotype distribution in Japanese patients with diabetes mellitus," <i>Intern. Med.</i> , 37:581-584, 1998.
/	C55	Shih <i>et al.</i> , "Mice lacking serum paraoxonase are susceptible to organophosphate toxicity and atherosclerosis," <i>Nature</i> , 394:284-287, 1998.
/	C56	Sidell, "Soman and sarin: clinical manifestations and treatment of accidental poisoning by organophosphates," <i>Clin. Toxicol.</i> , 7:1-17, 1974.
/	C57	Sorenson <i>et al.</i> , "Reconsideration of the catalytic center and mechanism of mammalian paraoxonase/arylesterase," <i>Proc. Nat'l Acad. Sci. USA</i> , 92:7187-7191, 1995.
/	C58	Sorenson <i>et al.</i> , "The genetic mapping and gene structure of mouse paraoxonase/arylesterase," <i>Genomics</i> , 30:431-438, 1995.
/	C59	Tucker, "Evidence Iraq used chemical weapons during the 1991 Persian Gulf War," <i>The Nonproliferation Review</i> , Spring-Summer:114-122, 1997.
/	C60	U.S. Senate Committee Report on Banking, Housing and Urban Affairs, United States Senate. U.S. chemical and biological warfare-related dual use exports to Iraq and their possible impact on the health consequences of the Persian Gulf War. Washington: U.S. Senate, 1994.
/	C61	Yokoyama <i>et al.</i> , "A preliminary study of delayed vestibulocerebellar effects of Tokyo subway sarin poisoning in relation to gender difference: frequency analysis of postural sway," <i>J. Occup. Environ. Med.</i> , 40:17-21, 1998.
/	C62	Yokoyama <i>et al.</i> , "Chronic neurobehavioral and central and autonomic nervous system effects of Tokyo subway sarin poisoning," <i>J. Physiol. Paris</i> , 92:317-323, 1998.

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